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known to confer the index phenotype and being genetically distinguishable from the founder inbred strain, wherein [some] at least one of the F<sub>1</sub> progeny that carry the dominant allele also carry at least one random mutation;

backcrossing [the] gametes from male F<sub>1</sub> progeny to at least one female of the index inbred strain, with or without the index allele, to obtain N2 backcross progeny, wherein at least [some] one of the N2 backcross progeny that carry the dominant allele also exhibit the outlying phenotype; and

verifying that the outlying phenotype is caused by a segregating mutation.

5. (Amended) A method as claimed in Claim 1 wherein the dominant allele is a *Min* allele at an *Apc* locus in a mouse.

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6. (Amended) A method as claimed in Claim 1 wherein the index inbred strain [is an isogenic index strain that carries] and the founder inbred strain share an isogenic genetic background but can be distinguished by single nucleotide polymorphisms.

11. (Amended) A method for identifying a segregating mutation at a genetic locus that modifies an index phenotype in [an] a non-human index inbred strain, the segregating mutation causing an outlying phenotype relative to the index phenotype, the method comprising the steps of:

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crossing a non-human founder inbred strain with [an] a non-human index inbred strain to obtain Gen1 progeny, the founder inbred strain carrying random point mutations relative to a wild-type animal of the founder inbred strain, the index inbred strain carrying a congenic dominant allele at a locus known to confer the index phenotype, the [allele being provided on a] founder strain and the index strain sharing an isogenic genetic background [of the wild-type founder inbred strain], wherein some of the Gen1 progeny that carry the dominant allele also exhibit a modified index phenotype; and

verifying that Gen1 progeny that carry the dominant allele and exhibit a modified index phenotype carry a segregating mutation.

16. (Amended) A method as claimed in Claim 15 wherein the genetically distinguishable inbred strain [is an inbred strain having the] shares an isogenic genetic background [of] with the [wild-type founder inbred strain] founder and index strains and further [comprising] comprises single nucleotide polymorphisms relative to the [wild-type] founder inbred strain.

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17. (Amended) A genetically altered mouse [having a genetic background characteristic of a first inbred mouse strain, the mouse] comprising in its genome:

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a congenic dominant heterozygous allele that confers an index phenotype on [a mouse having the characteristic genetic background] the mouse; [and]

a segregating modifier of the index phenotype, the modifier being [genetically linked to a genetic marker characteristic of a second inbred mouse strain] attributable to a single point mutation,

[wherein the index phenotype in the genetically altered mouse is modified relative to the index phenotype in a mouse that comprises the dominant allele on the genetic background characteristic of the first inbred mouse strain but which lacks the segregating modifier] and a single nucleotide mapping polymorphism genetically linked to the single point mutation.

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19. (Amended) A non-human animal comprising a segregating mutation that modifies an index phenotype, the animal being prepared according to a method comprising the steps of:

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outcrossing [a] at least one male animal of a founder inbred non-human strain to at least one female animal of an index inbred non-human strain to obtain F<sub>1</sub> progeny, the founder inbred strain carrying random point mutations relative to a wild-type animal of the founder inbred strain, the index inbred strain carrying a congenic dominant allele at a locus known to confer the index phenotype and being genetically distinguishable from the founder inbred strain, wherein [some] at least one of the F<sub>1</sub> progeny that carry the dominant allele also carry at least one random mutation;

backcrossing [the] gametes from male F<sub>1</sub> progeny to the index inbred strain, with or without the index allele, to obtain N2 backcross progeny, wherein at least [some] one of the N2 backcross progeny that carry the dominant allele also exhibit the outlying phenotype;

verifying that the outlying phenotype is caused by a segregating mutation; and

selecting an animal that shows the outlying phenotype.

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21. (Amended) A non-human animal comprising a segregating mutation that modifies an index phenotype, the animal being prepared according to a method comprising the steps of:

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crossing a founder inbred strain with an index inbred strain to obtain Gen1 progeny, the founder inbred strain carrying random point mutations relative to a wild-type animal of the founder inbred strain, the index inbred strain carrying a congenic dominant allele at a locus known to confer the index phenotype, the [allele being provided on a] founder strain and the index strain sharing an isogenic genetic background [of the wild-type founder inbred strain], wherein some of the Gen1 progeny that carry the dominant allele also exhibit a modified index phenotype;

verifying that Gen1 progeny that carry the dominant allele and exhibit a modified index phenotype carry a segregating mutation; and  
selecting an animal that shows the outlying phenotype.

Sub 25. (Amended) A method for identifying a segregating mutation at a genetic locus that modifies an index phenotype in [an] a non-human index inbred strain, the segregating mutation causing an outlying phenotype relative to the index phenotype, the method comprising the steps of:

outcrossing a non-human founder isogenic inbred strain with the non-human index inbred strain to obtain Gen1F<sub>1</sub> progeny, the founder isogenic strain being heterozygous only for random point mutations relative to a wild-type animal of the founder inbred strain, the index inbred strain carrying a dominant allele at a locus known to confer the index phenotype, where at least some of the Gen1F<sub>1</sub> progeny carry both the dominant allele and at least one random mutation;

crossing a founder animal of the founder isogenic inbred strain to an animal of the founder strain that lacks the mutations to obtain inbred Gen2 offspring, where the founder animal has at least one outcrossed F<sub>1</sub> progeny that displays the outlying phenotype relative to the index phenotype;

outcrossing Gen2 offspring to the index strain to obtain Gen2F<sub>1</sub> backcross progeny, half of which, on average, carry the dominant allele that confers the index phenotype; and  
verifying that a subset of the Gen2F<sub>1</sub> progeny shows the outlying phenotype.

#### REMARKS

In an Office Action mailed December 7, 1999, the Examiner in charge of the application maintained a requirement for restriction among Groups I, II and III but recombined Groups I and IV into the single group now being examined. Claims 1, 3, 5, 6, 11, and 17-25 were rejected for obviousness-double patenting. Claims 1-6, 11-16, 19-23, and 25 were rejected under 35 U.S.C. §112, first paragraph for overbreadth. Claims 1-6 and 11-25 were rejected under 35 U.S.C. §112, second paragraph, for indefiniteness. Claims 1, 3-6 and 11-25 were rejected under 35 U.S.C. §102(a) as being anticipated by Bilger et al. (1996). Claims 1, 3, 11, 17, and 19-25 were rejected under 35 U.S.C. §102(b) as being anticipated by Shedlovsky et al. (1986). Claims 2, 5, and 18 were rejected under 35 U.S.C. §103(a) over Shedlovsky et al. in view of Moser et al. (1990) and Dietrich et al. (1993).

Applicants respectfully traverse the rejections imposed and consider each such rejection separately below. In view of the amendments noted above and the arguments presented herein, applicants respectfully request reconsideration of the merits of this patent application.